

Patent  
Attorney's Docket No. 000510-007

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of )  
Staffan NILSSON et al ) Group Art Unit: Unassigned  
Application No.: Unassigned ) Examiner: Unassigned  
(Utility Application claiming priority to )  
Provisional Serial No. 60/262,420 )  
Filed: January 22, 2002 )  
For: A SCREENING SYSTEM )

**PRELIMINARY AMENDMENT**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Prior to examination on the merits, please enter the following amendments.

**IN THE CLAIMS:**

Kindly replace Claims 4-9, 13-19, 21 and 22, and add new claims 23-34, as follows.

4. (amended) The method according to claim 1, wherein the droplet is levitated using a levitator selected from the group consisting of an acoustic, electrostatic, air flow, magnetic levitator and any hybrids thereof.

5. (amended) The method according to claim 1, wherein the dispenser is a piezoelectric flow-through dispenser.

6. (amended) The method according to claim 1, wherein the substance delivered to the droplet is a protein, a membrane protein, a peptide, an enzyme, a receptor, a drug compound, nucleic acid, a macromolecule, macromolecular assembly or complexes thereof.

7. (amended) The method according to claim 1, wherein the substance delivered to the droplet is a substance influencing the nucleation conditions.

8. (amended) The method according to claim 1, wherein the droplet is in the range of 1 fl to 100  $\mu$ l.

9. (amended) The method according to claim 1, wherein the nucleation tendency is detected within the range of 10 milliseconds - 10 hours.

13. (amended) The system according to claim 12, wherein the levitator is selected from the group consisting of an acoustic, electrostatic, air flow, magnetic levitator and any hybrids thereof.

14. (amended) The system according to claim 12, wherein the dispenser is a piezoelectric dispenser.

15. (amended) The system according to claim 12, wherein the nucleation tendency is detected manually by visual surveillance.

16. (amended) The system according to claim 12, wherein the nucleation tendency is detected by any of the means selected from the group consisting of Raman spectroscopy, multi-angle light scattering in combination with Raman spectroscopy, nephelometry, and an illuminator source, to obtain a quantitative measurement of turbidity, precipitate and/or aggregate formation in the at least one droplet.

17. (amended) The system according to claim 12, wherein the at least one levitated droplet is in the range of 1 fl to 100  $\mu$ l.

18. (amended) The system according to claim 12, wherein the at least one substance delivered to the at least one droplet by the at least one dispenser is a protein, a membrane protein, a peptide, an enzyme, a receptor, a drug compound, nucleic acid, a macromolecule, macromolecular assembly or complexes thereof.

19. (amended) The system according to claim 12, wherein the at least one substance delivered to the at least one droplet by the at least one dispenser is a substance influencing nucleation tendency.

21. (amended) A method for screening crystallization conditions or amorphous stage conditions for a molecule, comprising  
using a system according to claim 12 to screen the crystallization conditions or amorphous stage conditions for the molecule.

22. (amended) A method for screening crystallization conditions or amorphous stage conditions for a molecule, comprising

- i. levitating at least one droplet of a fluid or gas in a levitator,
- ii. delivering at least one substance comprising the molecule to the levitating droplet with a dispenser for delivering the substance,
- iii. detecting the nucleation tendency, and
- iv. scoring the nucleation tendency.

Please add new claims 23-34 as follows:

-- 23. (new) The method according to claim 4, wherein the levitator is an acoustic-electrostatic hybrid levitator.

24. (new) The method according to claim 6, wherein the peptide is an oligopeptide or a polypeptide.

25. (new) The method according to claim 6, wherein the nucleic acid is DNA or RNA, an oligonucleotide, or a polynucleotide.

26. (new) The system according to claim 13, wherein the levitator is an acoustic-electrostatic hybrid levitator.

27. (new) The method according to claim 18, wherein the peptide is an oligopeptide or a polypeptide.

28. (new) The method according to claim 18, wherein the nucleic acid is DNA or RNA, an oligonucleotide, or a polynucleotide.

29. (new) The method according to claim 21, wherein the molecule is a protein, a membrane protein, a peptide, an enzyme, a receptor, a drug compound, nucleic acid, a macromolecule, macromolecular assembly or complexes thereof.

30. (new) The method according to claim 29, wherein the peptide is an oligopeptide or a polypeptide.

31. (new) The method according to claim 29, wherein the nucleic acid is DNA or RNA, an oligonucleotide, or a polynucleotide.

32. (new) The method according to claim 22, wherein the molecule is a protein, a membrane protein, a peptide, an enzyme, a receptor, a drug compound, nucleic acid, a macromolecular, macromolecular assembly or complexes thereof.

33. (new) The method according to claim 32, wherein the peptide is an oligopeptide or a polypeptide.

34. (new) The method according to claim 32, wherein the nucleic acid is DNA or RNA, an oligonucleotide, or a polynucleotide. - -

**REMARKS**

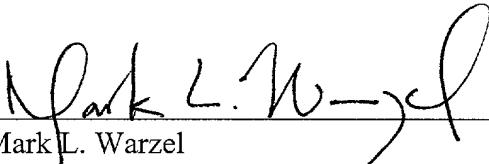
Entry of the foregoing, examination and consideration of the above-identified application, as amended, are respectfully requested.

By the foregoing amendment, Claims 4-9, 14-19, 21 and 22 been amended to remove multiple dependencies from the claims and to better conform to U.S. patent practice. New Claims 23-34 have been added to include claims directed to those aspects of Applicants' claimed invention that were removed from the original claims.

Favorable and early consideration on the merits is respectfully requested.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By:   
Mark L. Warzel  
Registration No. 47,264

P.O. Box 1404  
Alexandria, VA 22313-1404  
(703) 836-6620

Date: January 22, 2002

**Attachment to Preliminary Amendment Filed January 22, 2002**  
**Marked-up Version of Claims 4-9, 13-19, 21 and 22**

---

4. (amended) The method according to [any of claims 1-3] claim 1, wherein the droplet is levitated using a levitator selected from the group [selected] consisting of an acoustic, electrostatic, air flow, magnetic levitator and any hybrids thereof [, such as acoustic-electrostatic hybrid levitator].

5. (amended) The method according to [any of claims 1-4] claim 1, wherein the dispenser is a piezoelectric flow-through dispenser.

6. (amended) The method according to [any of claims 1-5] claim 1, wherein the substance delivered to the droplet is a protein, a membrane protein, a peptide, [such as an oligopeptide or a polypeptide,] an enzyme, a receptor, a drug compound, nucleic acid, [such as DNA or RNA; oligonucleotide, polynucleotide,] a macromolecule, macromolecular assembly or complexes thereof.

7. (amended) The method according to [any of claims 1-6] claim 1, wherein the substance delivered to the droplet is a substance influencing the nucleation conditions.

8. (amended) The method according to [any of claims 1-7] claim 1, wherein the droplet is in the range of 1 fl to 100  $\mu$ l.

9. (amended) The method according to [any of claims 1-8] claim 1, wherein the nucleation tendency is detected within the range of 10 milliseconds - 10 hours.

**Attachment to Preliminary Amendment Filed January 22, 2002**  
**Marked-up Version of Claims 4-9, 13-19, 21 and 22**

---

13. (amended) The system according to claim 12, wherein the levitator is selected from the group consisting of an acoustic, electrostatic, air flow, magnetic levitator and any hybrids thereof [, such as acoustic-electrostatic hybrid levitator].

14. (amended) The system according to [any of claims 12-13] claim 12, wherein the dispenser is a piezoelectric dispenser.

15. (amended) The system according to [any of claims 12-14] claim 12, wherein the nucleation tendency is detected manually by visual surveillance.

16. (amended) The system according to [any of claims 12-14] claim 12, wherein the nucleation tendency is detected by any of the means selected from the group consisting of Raman spectroscopy, multi-angle light scattering in combination with Raman spectroscopy, nephelometry, and an illuminator source, to obtain a quantitative measurement of turbidity, precipitate and/or aggregate formation in the at least one droplet.

17. (amended) The system according to [any of claims 12-16] claim 12, wherein the at least one levitated droplet is in the range of 1 fl to 100  $\mu$ l.

18. (amended) The system according to [any of claims 12-17] claim 12, wherein the at least one substance delivered to the at least one droplet by the at least one dispenser is a protein, a membrane protein, a peptide, [such as an oligopeptide or a polypeptide,] an enzyme, a receptor, a drug compound, nucleic acid, [such as DNA or RNA; oligonucleotide, polynucleotide,] a macromolecule, macromolecular assembly or complexes thereof.

**Attachment to Preliminary Amendment Filed January 22, 2002**  
**Marked-up Version of Claims 4-9, 13-19, 21 and 22**

19. (amended) The system according to [any of claims 12-17] claim 12, wherein the at least one substance delivered to the at least one droplet by the at least one dispenser is a substance influencing nucleation tendency.

21. (amended) [Use of a system according to any of claims 12-20,] A method for screening [crystallisation] crystallization conditions or amorphous stage conditions for a molecule [such as a protein, a membrane protein, a peptide, such as an oligopeptide or a polypeptide, an enzyme, a receptor, a drug compound, nucleic acid, such as DNA or RNA; oligonucleotide, polynucleotide, a macromolecule, macromolecular assembly or complexes], comprising

using a system according to claim 12 to screen the crystallization conditions or amorphous stage conditions for the molecule.

**Attachment to Preliminary Amendment Filed January 22, 2002**  
**Marked-up Version of Claims 4-9, 13-19, 21 and 22**

---

22. (amended) [Use of a method according to claim 1-11,] A method for screening [crystallisation] crystallization conditions or amorphous stage conditions for a molecule [such as a protein, a membrane protein, a peptide, such as an oligopeptide or a polypeptide, an enzyme, a receptor, a drug compound, nucleic acid, such as DNA or RNA; oligonucleotide, polynucleotide, a macromolecular, macromolecular assembly or complexes] ,comprising

- i. levitating at least one droplet of a fluid or gas in a levitator,
- ii. delivering at least one substance comprising the molecule to the levitating droplet with a dispenser for delivering the substance,
- iii. detecting the nucleation tendency, and
- iv. scoring the nucleation tendency.